individual patients' conditions, life expectancy, and values to inform an optimal individualized ICD implantation decision.

Sean D. Pokorney, MD, MBA
Eric D. Peterson, MD, MPH
Tracy Y. Wang, MD, MHS, MSc

Author Affiliations: Division of Cardiology, Duke University Medical Center, Durham, North Carolina.

Corresponding Author: Sean Pokorney, MD, MBA, Division of Cardiology, Duke University Medical Center, 2301 Erwin Rd, DUMC 3845, Durham, NC 27710 (sean.pokorney@duke.edu).

Conflict of Interest Disclosures: The authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Dr Pokorney reported receiving grants from the Agency for Healthcare Research and Quality, Boston Scientific, AstraZeneca, and Gilead; and receiving personal fees from Janssen Pharmaceuticals and Medtronic. Dr Peterson reported receiving grants from Janssen Pharmaceuticals, Eli Lilly, and the American Heart Association; and receiving personal fees from Janssen Pharmaceuticals, Bayer, Boehringer Ingelheim, Genentech, Merck, AstraZeneca, and Sanofi. Dr Wang reported receiving grants from the Agency for Healthcare Research and Quality, Boston Scientific, Eli Lilly, Daiichi Sankyo, Gilead, GlaxoSmithKline, AstraZeneca, Regeneron, and Bristol-Myers Squibb; serving as a consultant for AstraZeneca, Eli Lilly, and Premier; and receiving payment from Creative Educational Concepts and Rockpointe Corporation for continuing medical education presentations.

Disclaimer: Dr Peterson is an associate editor, *JAMA*, but was not involved in the editorial review of or decision to publish this letter.

1. Efficacy and safety of ICD implantation in the elderly (I-70). https://www.clinicaltrials.gov/ct2/show/NCT02121158. Accessed August 15, 2015.

2. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*. 1987;40(5):373-383.

3. Roe MT, Chen AY, Thomas L, et al. Predicting long-term mortality in older patients after non-ST-segment elevation myocardial infarction: the CRUSADE long-term mortality model and risk score. *Am Heart J*. 2011;162(5):875-883.e1.

4. Jain R, Duval S, Adabag S. How accurate is the eyeball test? a comparison of physician's subjective assessment versus statistical methods in estimating mortality risk after cardiac surgery. *Circ Cardiovasc Qual Outcomes*. 2014;7(1):151-156.

5. Devereaux PJ, Anderson DR, Gardner MJ, et al. Differences between perspectives of physicians and patients on anticoagulation in patients with atrial fibrillation: observational study. *BMJ*. 2001;323(7323):1218-1222.

Risk Prediction for Individuals

To the Editor A Viewpoint by Dr Sniderman and colleagues[1] discussed how risk estimates from prediction models should be interpreted in the era of predictive analytics. We would like to expand on 2 statements.

First, we disagree that "probability is not meaningful in an individual context." Historically, the concept of individual risk has been vigorously debated. This discussion arises from the fact that a patient will or will not develop the disease or experience the event of interest. However, risk can be thought of as the subjective level to which one "believes in" or is "prepared to bet on" the occurrence of a disease or event,[2] just as one bets on future 1-time events in games of sport. Acting on risk minimizes mistakes and maximizes clinical outcomes: one must play the odds to be successful.[3] Hence, risk assessment is highly meaningful for the individual.

Second, Sniderman and colleagues stated that risk models are uncertain about true individual risk. Indeed, risk models only provide an indication of risk for patients with similar predictor values, both when developed with modern predictive techniques or classic statistical regression analysis. We disagree with the implication that this limits the relevance of risk predictions for individuals because a little prediction goes a long way.[4]

Adding more and more predictors to the model may refine risk assessments, but crucial to the understanding of risk estimation is the idea of conditioning (ie, which pieces of information about the patient are known at a given time and were used in the predictive model). We suggest language such as "based on your age, risk factors, and noninvasive imaging, your risk of this cancer is 10%. This risk may be refined should you get an invasive biopsy."

Because models are imperfect, the calibration of risk estimates should be assessed carefully in validation studies by comparing estimated risk with observed outcomes. For example, among patients with an estimated disease risk of 10%, does 1 in 10 on average have the disease or experience the event? Calibration should receive more attention in epidemiological research because this property determines the model's potential clinical utility, in combination with the model's discriminative ability.[5]

Risk prediction is highly relevant for decision making. For application at the individual level, it is imperative that physicians and patients have a good understanding of the concept of risk as well as knowing what information was available to the risk model.

Ben Van Calster, PhD
Ewout W. Steyerberg, PhD
Frank H. Harrell, PhD

Author Affiliations: Department of Development and Regeneration, KU Leuven–University of Leuven, Leuven, Belgium (Van Calster); Department of Public Health, Erasmus MC–University Medical Center Rotterdam, Rotterdam, the Netherlands (Steyerberg); Department of Biostatistics, Vanderbilt University School of Medicine, Nashville, Tennessee (Harrell).

Corresponding Author: Ben Van Calster, PhD, Department of Development and Regeneration, KU Leuven, University of Leuven, Herestraat 46 Box 703, B-3000, Leuven, Belgium (ben.vancalster@med.kuleuven.be).

Conflict of Interest Disclosures: The authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none were reported.

1. Sniderman AD, D'Agostino RB Sr, Pencina MJ. The role of physicians in the era of predictive analytics. *JAMA*. 2015;314(1):25-26.

2. Nau RF. De Finetti was right: probability does not exist. *Theory Decis*. 2001;51(2):89-124.

3. Silver N. *The Signal and the Noise: Why So Many Predictions Fail—But Some Don't*. New York, NY: Penguin Press; 2012.

4. Siegel E. *Predictive Analytics: The Power to Predict Who Will Click, Buy, Lie, or Die*. Hoboken, NJ: John Wiley & Sons; 2013.

5. Van Calster B, Vickers AJ. Calibration of risk prediction models: impact on decision-analytic performance. *Med Decis Making*. 2015;35(2):162-169.

In Reply We agree with Dr Van Calster and colleagues that risk assessment is valuable in the care of individuals. We stated in the conclusion of our Viewpoint that "Predictive algorithms are an essential component of guideline recommendations." The phrase about probability not being meaningful in the individual context was misunderstood and not intended to imply that calculating individual risks was not useful.

Instead, we wanted to direct the reader to the excellent discussion by Cohen[1] of the limitations of the frequentist notion of probability understood as an estimate of the frequency of a particular event in a total sequence of events. Basically, we meant that frequentist probability is not verifiable in an individual context because a person either experiences or does not experience the event. Consequently, we agree that calibration is important in the assessment of predictive model performance.

We are pleased Van Calster and colleagues agree that risk estimates are uncertain about individual risk. This matters because many guidelines are applied in a binary fashion; therefore, if the risk estimate falls above or below a decision line, potentially lifesaving therapy will or will not be administered. We think that highlighting the limitations of individual risk will help clinicians treat the risk estimate as one important component in their practice of care and not a definitive assessment of their patient's future. This view is highlighted by the recent American Heart Association/American College of Cardiology cholesterol guidelines that consider risk assessment as the first step in an informed discussion between the patient and his or her physician.[2]

Van Calster and colleagues expand on our point about the conditional nature of risk estimates. Paraphrasing their suggested wording to our cardiovascular example, we would say "based on your age and standard risk factors, your risk of experiencing a cardiovascular event in the next 10 years is 10%. This risk may be refined should you obtain your coronary calcium." This presentation highlights the time horizon used as another limitation in the application of risk algorithms. Unlike their diagnostic cousins, prognostic models assess the risk of disease occurring in a prespecified future time. But treating 40- or 50-year-olds based solely on their 10-year risk of cardiovascular disease may be short-sighted because low risk may mask nonreversible detrimental changes occurring in the arterial wall.

We suggest that greater emphasis should be placed on the causal factors for the disease. In cardiovascular prevention, these factors are entered into all conventional algorithms, but compared with age and sex, they play little role in driving the resulting estimate. Thus, those with earlier, persistent elevations of cholesterol may be at much greater longer-term risk than those with intermittent elevations, but these important differences may not produce meaningfully different estimates of calculated 10-year risk.[3]

The limitations of prognostic models mean the physician must play a vital role in the decision-making process. As Silver put it, "The key is in remembering that a model is a tool to help us understand the complexities of the universe, and never a substitute for the universe itself."[4]

Allan D. Sniderman, MD
Ralph B. D'Agostino Sr, PhD
Michael J. Pencina, PhD

Author Affiliations: Royal Victoria Hospital, McGill University, Montreal, Quebec, Canada (Sniderman); Department of Mathematics and Statistics, Boston University, Boston, Massachusetts (D'Agostino Sr); Duke Clinical Research Institute, Duke University, Durham, North Carolina (Pencina).

Corresponding Author: Michael J. Pencina, PhD, Duke Clinical Research Institute, Department of Biostatistics and Bioinformatics, Duke University, 2400 Pratt St, Durham, NC 27705 (michael.pencina@duke.edu).

Conflict of Interest Disclosures: The authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Dr Pencina reported receiving personal fees from McGill University Health Center/Doggone Foundation. No other disclosures were reported.

1. Cohen LJ. *An Introduction to the Philosophy of Induction and Probability.* New York, NY: Oxford University Press; 1989.

2. Stone NJ, Robinson JG, Lichtenstein AH, et al; American College of Cardiology/American Heart Association Task Force on Practice Guidelines. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2014;63(25 pt B):2889-2934.

3. Navar-Boggan AM, Peterson ED, D'Agostino RB Sr, Neely B, Sniderman AD, Pencina MJ. Hyperlipidemia in early adulthood increases long-term risk of coronary heart disease. *Circulation*. 2015;131(5):451-458.

4. Silver N. *The Signal and the Noise: Why So Many Predictions Fail—But Some Don't.* New York, NY: Penguin Press; 2012.

Guidelines for Letters

Letters discussing a recent *JAMA* article should be submitted within 4 weeks of the article's publication in print. Letters received after 4 weeks will rarely be considered. Letters should not exceed 400 words of text and 5 references and may have no more than 3 authors. Letters reporting original research should not exceed 600 words of text and 6 references and may have no more than 7 authors. They may include up to 2 tables or figures but online supplementary material is not allowed. All letters should include a word count. Letters must not duplicate other material published or submitted for publication. Letters not meeting these specifications are generally not considered. Letters being considered for publication ordinarily will be sent to the authors of the *JAMA* article, who will be given the opportunity to reply. Letters will be published at the discretion of the editors and are subject to abridgement and editing. Further instructions can be found at http://jama.com/public/InstructionsForAuthors.aspx. A signed statement for authorship criteria and responsibility, financial disclosure, copyright transfer, and acknowledgment and the ICMJE Form for Disclosure of Potential Conflicts of Interest are required before publication. Letters should be submitted via the *JAMA* online submission and review system at http://manuscripts.jama.com. For technical assistance, please contact jama-letters@jamanetwork.org.

Section Editor: Jody W. Zylke, MD, Deputy Editor.